PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 2002/0076	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/CU 03/00004	International filing date *(day/month/year)* 11.04.2003	Priority date *(day/month/year)* 15.04.2002
International Patent Classification (IPC) or both national classification and IPC A61K38/18		
Applicant CENTRO DE INGENIERIA GENETICA Y BIOTECNOLOGIA ...		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
16.12.2003	27.10.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Merckling-Ruiz, V Telephone No. +49 89 2399-8590

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CU 03/00004

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-40 as originally filed

Claims, Numbers

1-68 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☒ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

   see separate sheet

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☐ claims Nos.

   because:

   ☒ the said international application, or the said claims Nos. 1-31 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	11-17,42-48,54,59-68
	No:	Claims	1-10,18-41,49-53,55-58
Inventive step (IS)	Yes:	Claims	11-17,42-48,54,59-68
	No:	Claims	1-10,18-41,49-53,55-58
Industrial applicability (IA)	Yes:	Claims	32-68 (YES), 1-31 see separate sheet
	No:	Claims	

2. Citations and explanations

   see separate sheet

1. Reference is made to the following documents :

D1: WO 00/53219 A (MADSEN JOHN ;ENTREMED INC (US); HOLADAY JOHN W (US); RUIZ ANTONIO) 14 September 2000 (2000-09-14)

D2: WEI, Y-Q ET AL.: "Immunogene therapy of tumors with vaccine based on Xenopus homologous vascular endothelial growth factor as a model antigen." PNAS, vol. 98, no. 20, September 2001 (2001-09), XP002248645

D3: DAVIDOFF, A.M. ET AL.: "Bone marrow-derived cells contribute to tumor neovasculature and, when modified to express an angiogenesis inhibitor, can restrict tumor growth in mice." CLINICAL CANCER RESEARCH, vol. 7, September 2001 (2001-09), XP002248646

D4: PREWETT, M. ET AL.: "Antivascular endothelial growth factor receptor (fetal liver kinase 1) monoclonal antibody inhibits tumor angiogenesis and growth of several mouse and human tumors." CANCER RESEARCH, vol. 59, October 1999 (1999-10), XP002248647

Regarding point I

2. In amended claims 1-79 filed with the letter of 10.09.04, no support was given for the amendments. It appears that at least some of the amendments are not supported by the application as filed. For example, there is no explicit disclosure of a composition comprising a combination of VEGFR and VEGF (as in claims 23-25). The present opinion is therefore based on the set of claims 1-68 as originally filed.

Regarding point III

2. Claims 1-31 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Regarding point V

3. For the assessment of the present claims 1-31 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

4. D1 discloses immunogenic compositions comprising the receptor-binding domain of VEGF and their use for preventing or treating cancer and other hyperproliferative diseases (see claims 11, 17, 22, 27, 40, pages 5-6 and page 9 lines 26-34).
D2 is directed to tumor therapy through active immunotherapy with a vaccine based on VEGF from Xenopus (see abstract, page 11546 right col. and page 11550 right col.).
These documents anticipate the subject-matter of claims 1-10, 18-41, 49-53 and 55-58.

4.1 The documents cited in the search report do not disclose or suggest the use of :
- antigens based on a peptide other than VEGF-A
- adjuvants
- mixtures of several antigens.

Claims 11-17, 42-48, 54 and 55-68 would thus prima facie appear to be novel and inventive.

However, the applicant's attention is drawn to the fact that the search report does not seem to cite all the documents that would be relevant for the present application. As an example, the following documents (among many others describing the use of various VEGF or VEGFR peptides as anticancer vaccines) would also appear to be relevant and would be used for assessing novelty and/or inventive step in the regional phase :

WO-A-03062788
WO-A-0157067
Eriksson et al. (2002) XP002967596.

The applicant should be aware that the present opinion would be revised, at least in European countries, when entering the regional phase.